UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,846	11/21/2005	Alexander Alan Morley	18857	8971

272 7590 09/24/2008

SCULLY, SCOTT, MURPHY & PRESSER, P.C.
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
09/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,846	MORLEY ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,13,15-17,20,28,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 13, 15-17, 20, 28, 30, and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/02/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 5, 13, 15-17, 20, 28, 30, and 31 are pending and examined on the merits.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office Action is in reply to Applicants' correspondence of 6/30/2008.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put the application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is made **FINAL**.

Information Disclosure Statement

1. The Information Disclosure Statement of 05/02/2008 has been considered.

Withdrawn Claim Objections

2. The objection to claims 8, 9, 11-13, 15, 26-28, 30 and 31 under 37 CFR 1.75(c) as being in improper form, as set forth in the previous Office Action, is **WITHDRAWN** in light of the amendments to the claims.

3. The objections to claims 4 and 7, as set forth in the previous Office Action, are **WITHDRAWN** in light of the cancellation of claims 4 and 7.

Withdrawn Claim Rejections - 35 USC § 112 2nd ¶ - Indefiniteness

4. The rejections of claims 1, 2-7, 10, 14, 16, 17-25 and 39, as set forth in the previous Office Action, as unclear over recitations of 'the subject nucleic acid regions derived from said sample' as recited in claim 1, are **WITHDRAWN** in light of the amendments to the claims.

The rejections of claims 4, 5, 7, 14, and 16, as set forth in the previous Office Action, as unclear over recitations of the term 'corresponds', are **WITHDRAWN** in light of the amendments to the claims.

The rejections of claims 2-7, 10, 14, 16-25 and 39, as set forth in the previous Office Action, as are unclear over recitation of the purpose of the claimed methods for 'diagnosing and/or monitoring a clonal population of cells', as recited in the preamble of claims, is **WITHDRAWN** in light of the amendments to the claims and Applicants' arguments (p.6 of Remarks) that the skilled artisan would recognize that detection of nucleic acids 'indicative of the presence of a clonal population of cells' accomplishes the purpose of the methods as stated in the preambles of instant claims 2 and 17.

Withdrawn Claim Rejections - 35 USC § 102

5. The rejection of claims 1-5, 17-20, 23, 24 under 35 U.S.C. 102(b), as set forth in the previous Office Action, as being anticipated by Greiner et al (1995), is **WITHDRAWN** in light of the amendments to the claims to require the detection of mitochondrial DNA.

Maintained Claim Rejections - 35 USC § 103

Newly Applied to Claims as Necessitated by Amendment

6. Claims 1-2, 5, 13, 15-17, 20, 28, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greiner et al (1995) in view of Nomoto et al (2002).

Regarding claim 1, the reference teaches detecting a clonal population of cells in leukemias. The method of Greiner et al comprises co-localizing nucleic acids derived from the subject (Fig. 2; p.49, right col., lns.1-25) in a DGGE analysis, where a DGGE analysis is based on nucleotide sequence identity, and detecting the level of co-localization based on the presentation of a discrete band or a smear on a gel (Fig 5). The reference teaches that co-localization higher than a background level is indicative of the presence of the clonal cell population (e.g: Fig 5; Fig 7; and p.47, right col., lns. 35-39).

Relevant to claim 2, the methods of Greiner et al, as detailed in the previous paragraph of this Office Action, monitor a clonal population of cells at least in so far as the methods detect the population, where detection is monitoring. Additionally relevant to the limitations of the rejected claim, Greiner et al teaches the analysis of nucleic acids derived from a biological sample from a mammal (e.g. p.47, right col., ln.45 – p.48, left col., ln.15).

Regarding claim 5, Greiner et al teaches the analysis of cells from acute lymphoblastic leukemia (ALL) samples.

Regarding claims 15,16, 30 and 31, the method of Greiner et al comprises co-localizing nucleic acids derived from the subject (Fig. 2; p.49, right col., lns.1-25) in a

DGGE analysis (relevant to part (i) of claims 15 and 30), which is a denaturing gel electrophoresis (claims 16 and 31).

Regarding claim 17, Greiner et al teaches a method for monitoring ALL (where ALL is a leukemia and is a disease condition characterized by a clonal population of cells characterized by diagnostically distinct nucleic acid regions), at least in so far as the methods detect the clonal population of cells, where detection is monitoring. The reference teaches detecting a clonal population of cells. The method of Greiner et al comprises co-localizing nucleic acids derived from the subject (Fig. 2; p.49, right col., lns.1-25) in a DGGE analysis, where a DGGE analysis is based on nucleotide sequence identity, and detecting the level of co-localization based on the presentation of a discrete band or a smear on a gel (Fig 5). The reference teaches that co-localization higher than a background level is indicative of the presence of the clonal cell population (e.g: Fig 5; Fig 7; and p.47, right col., lns. 35-39).

Regarding claim 20, Greiner et al teaches the analysis of cells from acute lymphoblastic leukemia (ALL) samples.

Greiner et al does not specifically teach methods comprising the detection of mitochondrial DNA (claims 1, 2, and 17) or specifically the D loop (as required for claims 13 and 28). However the analysis of such elements in the analysis of clonal populations in cancer were well known in the art at the time the invention was made.

Nomoto et al teaches the analysis of clonal cell populations in cancer.

Relevant to the limitations of independent claims 1, 2, and 17, and dependent claims 13 and 28, Nomoto et al teaches the analysis of several polymorphic loci in the

mitochondrial D loop (Table 1) to determine clonality of cancer cells (p.481 – Experimental design).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the polymorphic D loop sequences of Nomoto et al in an analysis of ALL by the methods as set forth in Greiner et al. One would have been motivated to examine the nucleotide sequences of Nomoto et al based on the teaching of Nomoto et al (p.481, right col., last ¶) that the high frequency of mutations in the control region of mitochondrial DNA provides a tool to determine the clonal origin of multiple cancers in individual patients.

Response to Remarks

Applicants have traversed the rejection of claims as obvious in view of the teachings of Greiner et al in view of Nomoto et al. Applicants' arguments have been fully and carefully considered but are not found to be persuasive.

Applicants have argue that the primary reference of Greiner et al does not provide for the analysis of diagnostically distinctive DNA segments suitable for the identification of clonal populations where the reference teaches analysis of TCR-gamma DNA (Remarks p.8). The argument is not persuasive as the reference specifically teaches that amplification of TCR-gamma DNA and its analysis allows for the establishment of a DNA fingerprint of a clonal TCR-gamma DNA region (p.54, left col.).

Applicants further argue (p.10-11 or Remarks) that Nomoto et al does not teach the analysis of DNA using co-localization. The argument is not found to be persuasive,

as the Examiner has not relied upon Nomoto et al for any teaching of co-localization analysis, which the Examiner maintains is provided by Greiner et al.

Finally, Applicants argue that Nomoto et al is directed to a disease condition characterized by specific mutations. This is not found to be persuasive. Nomoto et al does not teach that detected D-loop mutations are causative specifically of hepatocellular carcinoma, but instead offers a general teaching that D-loop mutations allow for the identification of the monoclonal origin of tumor tissue (p.486, left col., lat two paragraphs).

The rejection as set forth is **MAINTAINED**.

Conclusion

7. No claim is allowable or free of the teachings of the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Stephen Kapushoc/
Art Unit 1634

/Jehanne S Sitton/
Primary Examiner, Art Unit 1634